necessitated by the phagemid approach because fusion with the infective N-terminal domain would render the host cell resistant to infection. The result is a phage-displaying antibody combining sites ("Phabs"). The antibody combining sites, such as Fab fragments, are displayed on the phage coat. This technique may be used to produce Phabs which display recombinantly produced Fab fragments, such as recombinantly produced Fab fragments that immunoreact with a antigen, on the phage coat of a filamentous phage such as M13.

## Remarks

This Supplemental Preliminary Amendment and the above-referenced SEQUENCE LISTING are filed to conform the above-referenced application to the requirements of 37 C.F.R. §§ 1.821 - 1.825. In accordance with 37 C.F.R. § 1.821(e), a copy of the above-submitted SEQUENCE LISTING in ASCII computer readable form is also submitted herewith. The contents of the paper version of the SEQUENCE LISTING and the computer readable form being submitted herewith are the same and do not include new matter.

The amendment to page 21 of the specification adding a sequence identifier and the amendments to Figure 5B changing three sequence identifiers are made to conform the above-referenced application to the requirements of 37 C.F.R. § 1.821(d).

Respectfully submitted,
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By their Representatives,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 20 day of September, 2001.

Name Emily Legendre

Signature Emily Legendre

**Clean Version of the Paragraph Spanning Pages 21-22**

AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR PARTICIPATION IN AUTOIMMUNE DISEASE
Applicant: Henrik Ditzel et al.
Serial No.: 09/828,708

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A phagemid vector may be constructed to fuse the antibody fragment chain such as an Fab, Fab' or preferably an Fd chain with the C-terminal domain of cpIII (see Barbas et al., Proc. Natl. Acad. Sci. USA, 88, 7978 (1991)). A flexible five-amino acid tether (GGGGS) (SEQ ID NO:123), which lacks an ordered secondary structure, may be juxtaposed between the expressed fragment chain and cpIII domains to minimize interaction. The phagemid vector may also be constructed to include a nucleotide coding for the light chain of a Fab fragment. The cpIII/Fd fragment fusion protein and the light chain protein may be placed under control of separate lac promoter/operator sequences and directed to the periplasmic space by pelB leader sequences for functional assembly on the membrane. Inclusion of the phage F1 intergenic region in the vector allows for packaging of single-stranded phagemid with the aid of helper phage. The use of helper phage superinfection may result in expression of two forms of cpIII. Consequently, normal phage morphogenesis may be perturbed by competition between the cpIII/Fd fragment fusion protein and the native cpIII of the helper phage for incorporation into the virion. The resulting packaged phagemid may carry native cpIII, which is necessary for infection, and the fusion protein including the Fab fragment, which may be displayed for interaction with an antigen and used for selection. Fusion at the C-terminal domain of cpIII is necessitated by the phagemid approach because fusion with the infective N-terminal domain would render the host cell resistant to infection. The result is a phage-displaying antibody combining sites ("Phabs"). The antibody combining sites, such as Fab fragments, are displayed on the phage coat. This technique may be used to produce Phabs which display recombinantly produced Fab fragments, such as recombinantly produced Fab fragments that immunoreact with a antigen, on the phage coat of a filamentous phage such as M13.

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